

Grave Familial Jaundice of the Newly Born.

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B*BRIEF Description.*—In grave familial jaundice, successive infants become jaundiced a few hours to a day after birth, pass into a drowsy condition, and usually die within a week, often with convulsions; it resembles physiological jaundice in its onset, and, like it, does not show any gross post-mortem appearances to account for the jaundice.

Pathogeny.—Pfannenstied regarded it as only an intensive form of the physiological jaundice, but not only is the prognosis very different, but there may be evidence of maternal toxæmia during the pregnancy. In three (Nason, Tylecote, Rolleston) out of the 25 family groups that I have collected—that is, in 15 out of 130 cases of newly-born infants with grave familial jaundice—the mothers had recurrent jaundice during their pregnancies. In the families reported by Smith and by Ritchie, the mothers had jaundice at the birth of one of the children, and in Arkwright's family of 14 cases with four recoveries the mother had had jaundice when four years old and was always "sallow." In Blomfield's cases, the mother suffered much from severe vomiting during the pregnancies, but this association appears to be exceptional. Against

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the view that this grave disease is due to maternal toxæmia, and that in its most complete form the mother is jaundiced as well as the child, it might be argued that, as a rule, the infants suffer much more than the mothers and that the jaundice does not appear until after birth; but it is obvious that similar objections might be raised to the transmission of congenital syphilis; and it may be added that in congenital obliteration of the bile ducts there is a similar or greater delay in the onset of jaundice. The following observation is perhaps in favour of the existence of maternal toxæmia :—

I gave the mother, who had had recurrent jaundice in three successive pregnancies with fatal familial jaundice in the infants, hexamine and salicylate of sodium in her fourth pregnancy; in the eighth month, she became somewhat jaundiced just before the birth of a boy who was never icteric and was well ten years later. During her fifth pregnancy she was treated by Dr. Spencer Lewis with small doses of hydrargyrum cum cretâ but was jaundiced during the eighth and ninth months of pregnancy, and bore a girl who was slightly jaundiced and died of acute summer gastro-enteritis when seven weeks old.

Benedict's cases of recurrent jaundice, with pruritus and hepatic enlargement, in two sisters during their pregnancies, these manifestations passing off after abortion or premature delivery and the offspring escaping icterus, might perhaps be regarded as incomplete cases and corresponding in this respect with the cases in which the offspring alone are jaundiced. It is highly desirable that the metabolism of the mothers of infants with familial jaundice should be thoroughly investigated, especially during their pregnancies. In the meanwhile, it is suggested that *in its most complete form the disease is hereditary, the mothers becoming jaundiced during the pregnancies of jaundiced infants, and that the usual familial form is an incomplete manifestation of the morbid processes.*

Ætiology.—Some of the families, in which the disease has been reported, are remarkable for the large number

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of pregnancies; in Arkwright's there were 15; in Auden's, 12; in Underwood's and Ritchie's, 11, and in Busfield's, Nason's, and Morris's, 10. Occasionally there are some miscarriages or premature births, but all the 11 pregnancies in the family reported by Ritchie went to full term. Some writers refer to the robust condition of the infants; but all Arkwright's cases were rather weakly, and one had an intra-uterine amputation of the forearm.

The disease appears to be less likely to attack the first and second born than the later infants in the families affected. The first-born escaped in the families reported by Arkwright, Smith, Auden, Busfield, McGibbon, Morris, Tylecote, Still (two families), and the first two children in those reported by Abt (two families), Duguid, Nason, and Ashby and Wright. The first-born therefore escaped in 14 out of the 25 families collected, and in several families the first-born was slightly jaundiced and was the only one to recover. There is no evidence that syphilis plays any part in the disease, and though infection has been put forward as a cause, there is no good reason to accept this.

The sex is not mentioned in some of the reports, but in those that I have collected there were 31 males and 31 females. The sex incidence thus differs from that of congenital hypertrophy of the pylorus and of congenital obliteration of the bile ducts, which are both, especially the former, much commoner in the male sex. It has occurred in twins (Still).

Morbid Anatomy.—There is bile-staining of most of the tissues, and, as in physiological jaundice, there is selective staining of the lenticular and other nuclei in the brain, while the cortex escapes. Punctate hæmorrhages in the viscera are described, but their importance is doubtful, for they are not uncommon in stillborn children. There is no gross obstruction of the bile-

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ducts in the recorded cases except in one of McGibbon's cases, described in detail by Buchan and Cowrie, in which there was obstruction but not obliteration of the biliary papilla.

Clinical Features.—Afebrile jaundice usually appears a few hours to a day or two after birth, and increases; but, as in other forms of jaundice, may show curious variations. The infants may be born icteric; Smith describes a jaundiced stillborn child, and noticed in his three cases that the liquor amnii and membranes were bile-stained. The stools are not acholic; the urine may or may not contain bile. Hæmorrhages are not a feature of the disease. In a few instances enlargement of the liver and spleen has been present. The infant becomes drowsy, and usually death occurs within the first 14 days, often during the first week, and commonly with convulsions. Recovery after prolonged drowsiness appears to be more likely to occur in the earlier infants of the family; in nearly all the reported cases of this familial jaundice the recovery has been complete; one of Morris's cases, a girl, survived for $4\frac{1}{2}$ years, and was jaundiced practically all the time.

Prognosis.—This is bad; out of 130 collected cases 100, or 77 per cent., proved fatal. It is possible that prophylactic treatment of the pregnant mother (*vide* p. 7) may improve the outlook in the future. Spiller has recorded four cases of spastic diplegia following recovery from severe jaundice in the newly-born, but none of these was stated to be of the grave familial form. In connection with this and with the selective staining ("kernicterus") of the cerebral nuclei in grave familial and in physiological jaundice of the newly-born, it is interesting to recall Wilson's comparison with the selective action of a poison, probably non-microbic and possibly a lipoid, causing bilateral degeneration of the lenticular nucleus in the disease progressive lenticular degeneration, which is constantly

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associated with hepatic cirrhosis of the portal, not of the biliary, type and is often familial.

Diagnosis.—Reference may be made here to the other forms of jaundice in the newly-born.

Simple, Physiological, or Idiopathic Jaundice has been estimated to occur in from 33 per cent. upwards of all births. Breschet believes that it is universal, and Bang found that the blood in the umbilical vein always contains bilirubin and that the amount of bile in the blood of the newly-born increases up to the third day of life, after which it begins to diminish. The jaundice begins within the first two days, and appears earlier than in the cases of grave infective jaundice. There are no symptoms, though sleepiness is mentioned by Langmead. No treatment is necessary, and the main points of interest about these cases are (a) in the first place, the differentiation at an early stage from the rare condition of grave familial jaundice, which depends on the history of the family, and (b) in the second place, the causation.

Congenital Obliteration of the Bile Ducts is accompanied by hepatic and splenic enlargement, and practically always proves fatal within eight months; it is, therefore, relatively chronic as compared with grave familial jaundice. It is not a familial disease, but the first case of grave familial jaundice in a family would be very difficult to distinguish during life from one of congenital obliteration of the ducts; hepatic and splenic enlargement and acholic stools would be in favour of gross obstruction. The pathogeny of congenital obliteration of the bile ducts has been much discussed. It is generally agreed that it is not due to syphilis, though there are a few cases (Beck, Simonini, Rolleston) of congenital syphilitic stricture of the common bile duct on record. John Thomson, Milne, and Lavenson consider that there is in the first instance a developmental aplasia or

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narrowing of the ducts which gives rise to obstructive cirrhosis. My own view is that a maternal toxæmia causes cirrhosis followed by a descending obliterative cholangitis; and Dr. S. Wyard suggests that there is an ascending cholangitis from the duodenum set up by the irritation exerted by the swallowed liquor amnii. Most writers agree that all cases are not necessarily due to the same mechanism.

The Severe Infective Forms of Jaundice, such as those due to umbilical, cutaneous, or intestinal infection, formerly occurred in epidemics, and were responsible in the old insanitary lying-in hospitals for a terrible mortality, but, as far as I know, are rare now. The jaundice comes on about the fifth day of life, or later than in familial jaundice, and is accompanied by signs of grave septicæmia, high fever, and hæmorrhages especially from the umbilicus or the alimentary canal. Winckel's disease (epidemic hæmoglobinuria with bronzing of the skin) and Buhl's disease (acute fatty degeneration) are manifestations of this septicæmia of the newly-born, the infection probably entering from the intestines. The prognosis is very grave. Treatment should consist in the administration of antistreptococcic serum, washing out the bowel, and the oral administration of intestinal antiseptics such as minute doses of calomel.

In Melæna Neonatorum jaundice is often present; thus Pitfield records as hæmophilia four successive males with jaundice and hæmorrhages.

Congenital Splenomegalic Hæmolytic Jaundice runs a mild course, and can hardly be called a disease; it is recognized by the characteristic fragility of the red blood corpuscles when tested with hypotonic solutions of salt. *Congenital syphilis* does not often cause jaundice; it usually comes on early and is accompanied by other signs of the disease such as enlargement of the liver and spleen. Secondary

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pyogenic infection may occur in these cases.

Treatment.—On the hypothesis that grave familial jaundice of the newly-born is due to foetal toxæmia of maternal origin, the prophylaxis should consist in care of the mother's diet and the administration of intestinal and biliary antiseptics, such as hexamine, salicylate of sodium, minute doses ($\frac{1}{20}$ gr.) of calomel, tetrachloride of naphthaline, salol, and guaiacol. Ballantyne recommends chloride of calcium.

The infant should be treated with small doses of calomel, which some authors consider to have done good, and should not be given the breast.

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